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IN THE CLAIMS:

Please cancel claims 31-38 ✓

✓ Please add the following claims

59. An array of oligonucleotide probes immobilized on a solid support, the array comprising at least two sets of oligonucleotide probes,

(1) a first probe set comprising a plurality of probes, each probe exactly complementary to a subsequence of a reference sequence, the segment including at least one interrogation position complementary to a corresponding nucleotide in the reference sequence,

(2) a second probe set comprising a corresponding probe for each probe in the first probe set, the corresponding probe in the second probe set being identical to the corresponding probe from the first probe set, except that the at least one interrogation position is occupied by a different nucleotide in each of the two corresponding probes from the first and second probe sets;

wherein the probes in the first probe set have at least three interrogation positions respectively corresponding to each of three contiguous nucleotides in the reference sequence;

provided that the array does not contain a complete set of probes of a given length.

60. An array of oligonucleotide probes immobilized on a solid support, the array comprising at least four sets of oligonucleotide probes,

(1) a first probe set comprising a plurality of probes, each probe exactly complementary to a subsequence of a reference sequence, the segment including at least one interrogation position complementary to a corresponding nucleotide in the reference sequence,

(2) second, third and fourth probe sets, each comprising a corresponding probe for each probe in the first probe set, the probes in the second, third and fourth probe sets being identical to the corresponding probe from the first probe set that includes the at least one interrogation position, except that the at least one interrogation position is occupied by a different nucleotide in each of the four corresponding probes from the four probe sets;

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provided the array lacks a complete set of probes of a given length.

61. The oligonucleotide array of claim 60, further comprising a fifth probe set comprising a corresponding probe for each probe in the first probe set, the corresponding probe from the fifth probe set being identical to the corresponding probe from the first probe set, except that the at least one interrogation position is deleted in the corresponding probe from the fifth probe set.

62. The oligonucleotide array of claim 61, further comprising a sixth probe set comprising a corresponding probe for each probe in the first probe set, the corresponding probe from the sixth probe set being identical to the corresponding probe from the first probe set, except that an additional nucleotide is inserted adjacent to the at least one interrogation position in the corresponding probe from the first probe set.

63. The array of claim 60 wherein the first probe set has at least three interrogation positions respectively corresponding to each of three contiguous nucleotides in the reference sequence.

64. The array of claim 59, wherein the first probe set has at least 50 interrogation positions respectively corresponding to each of 50 contiguous nucleotides in the reference sequence.

65. The oligonucleotide array of claim 59, wherein the array has between 100 and 100,000 probes.

66. The oligonucleotide array of claim 59, wherein the probes are linked to the support via a spacer.

67. The oligonucleotide array of claim 59, wherein the probes of the first probe set are 9-21 nucleotides long.

68. The array of claim 60, wherein the first probe set has at least 50 interrogation positions respectively corresponding to each of 50 contiguous nucleotides in the reference sequence.

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69. The oligonucleotide array of claim 60, wherein the array has between 100 and 100,000 probes.

70. The oligonucleotide array of claim 60, wherein the probes are linked to the support via a spacer.

71. The oligonucleotide array of claim 60, wherein the probes of the first probe set are 9-21 nucleotides long.

72. An array of oligonucleotide probes immobilized on a solid support, the array comprising at least one pair of first and second probe groups, each group comprising a first and second sets of oligonucleotide probes as defined by claim 59;

wherein each probe in the first probe set from the first group is exactly complementary to a subsequence of a first reference sequence and each probe in the first probe set from the second group is exactly complementary to a subsequence from a second reference sequence.

73. The array of claim 72, wherein the second reference sequence is a mutated form of the first reference sequence.

74. The array of claim 72, wherein each group further comprises third and fourth probe sets, each comprising a corresponding probe for each probe in the first probe set, the probes in the second, third and fourth probe sets being identical to a sequence comprising the corresponding probe from the first probe set or a subsequence of at least three nucleotides thereof that includes the interrogation position, except that the interrogation position is occupied by a different nucleotide in each of the four corresponding probes from the four probe sets.

75. The array of claim 72 that comprises at least forty pairs of first and second probe groups, wherein the probes in the first probe sets from the first groups of the forty pairs are exactly complementary to subsequences from forty respective first reference sequences.

76. A block of oligonucleotide probes immobilized on a solid support, comprising:

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a perfectly matched probe exactly complementary to a subsequence of a reference sequence, the segment having a plurality of interrogation positions respectively corresponding to a plurality of nucleotides in the reference sequence,

for each interrogation position, three mismatched probes, each identical to the perfectly matched probe, except in the interrogation position, which is occupied by a different nucleotide in each of the three mismatched probes and the perfectly matched probe;

provided the array lacks a complete set of probes of a given length.

77. The array of claim 76, wherein the segment of the perfectly matched probe comprises 3-20 interrogation positions corresponding to 3-20 respective nucleotides in the reference sequence.

78. An array of probes immobilized to a solid support comprising at least two blocks of probes, each block as defined by claim 76, a first block comprising a perfectly matched probe comprising a segment exactly complementary to a subsequence of a first reference sequence and a second block comprising a perfectly matched probe comprising a segment exactly complementary to a subsequence of a second reference sequence.

79. The array of claim 78, wherein the first reference sequence is from a wildtype gene and the second reference sequence is from a mutant gene.

80. The array of claim 78, comprising at least 10-100 blocks of probes, each comprising a perfectly matched probe comprising a segment exactly complementary to a subsequence of at least 10-100 respective reference sequences.

81. An array of oligonucleotide probes immobilized on a solid support, the array comprising at least four probes:

a first probe comprising first and second segments, exactly complementary to first and second subsequences of a reference sequence, the segments including at least one interrogation position corresponding to a nucleotide in the reference sequence, wherein either (1) the first and second subsequences are noncontiguous, or (2) the first and second subsequences are contiguous and the first and second segments are inverted relative to the complement of the first and second subsequences in the reference sequence;

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second, third and fourth probes, identical to a sequence comprising the first probe, except in the at least one interrogation position, which differs in each of the probes; provided the array lacks a complete set of probes of a given length.

82. A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

(a) hybridizing a sample comprising the target nucleic acid to an array of oligonucleotide probes immobilized on a solid support, the array comprising:

(1) a first probe set comprising a plurality of probes, each probe exactly complementary to a subsequence of the reference sequence, the segment including at least one interrogation position complementary to a corresponding nucleotide in the reference sequence,

(2) a second probe set comprising a corresponding probe for each probe in the first probe set, the corresponding probe in the second probe set being identical to the corresponding probe from the first probe set that includes the at least one interrogation position, except that the at least one interrogation position is occupied by a different nucleotide in each of the two corresponding probes from the first and second probe sets;

wherein, the probes in the first probe set have at least three interrogation positions respectively corresponding to each of at least three nucleotides in the reference sequence, and

(b) detecting a hybridization pattern of the oligonucleotide probes to the target nucleic acid and determining from the hybridization pattern whether a nucleotide in the target sequence is the same or different from the corresponding nucleotide in the reference sequence.

83. The method of claim 82, wherein the determining comprises comparing the hybridization pattern to the target nucleic acid with a hybridization pattern of a nucleic acid having the reference sequence to the array of oligonucleotide probes.

84. The method of claim 82, wherein the determining step comprises:

(1) comparing the relative specific binding of two corresponding probes from the first and second probe sets;

(2) assigning a nucleotide in the target sequence as the complement of the interrogation position of the probe having the greater specific binding;

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(3) repeating (1) and (2) until each nucleotide of interest in the target sequence has been assigned.

85. The method of claim 82, wherein the array further comprises third and fourth probe sets, each comprising a corresponding probe for each probe in the first probe set, the probes in the second, third and fourth probe sets being identical to the corresponding probe from the first probe set, except that the at least one interrogation position is occupied by a different nucleotide in each of the four corresponding probes from the four probe sets.

86. The method of claim 85, wherein the determining comprises comparing the hybridization pattern of the target nucleic acid with a hybridization pattern of a nucleic acid having the reference sequence to the oligonucleotide probes.

87. The method of claim 85, wherein the determining comprises:

- (1) comparing the relative specific binding of four corresponding probes from the first, second, third and fourth probe sets;
- (2) assigning a nucleotide in the target sequence as the complement of the interrogation position of the probe having the greatest specific binding;
- (3) repeating (1) and (2) until each nucleotide of interest in the target sequence has been assigned.

88. A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

- (a) hybridizing the target nucleic acid to an array of oligonucleotide probes immobilized on a solid support, the array comprising:
- a perfectly matched probe exactly complementary to a subsequence of a reference sequence, the segment having a plurality of interrogation positions respectively corresponding to a plurality of nucleotides in the reference sequence,
- for each interrogation position, three mismatched probes, each identical to the perfectly matched probe including the plurality of interrogation positions, except in the interrogation position, which is occupied by a different nucleotide in each of the three mismatched probes and the perfectly matched probe;
- (b) for each interrogation position,

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- (1) comparing the relative specific binding of the three mismatched probes and the perfectly matched probe;
- (2) assigning a nucleotide in the target sequence as the complement of the interrogation position of the probe having the greatest specific binding.

89. The method of claim 88, wherein the target sequence has an undetermined substitution relative to the reference sequence, and the method assigns a nucleotide to the substitution.

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90. A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

hybridizing the target sequence to the array of claim 72;

determining which probes in the first group, relative to one another, hybridize to the target sequence, the relative specific binding of the probes indicating whether the target sequence is the same or different from the first reference sequence;

determining which probes in the second group, relative to one another, hybridize to the target sequence, the relative specific binding of the probes indicating whether the target sequence is the same or different from the second reference sequence.

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91. The method of claim 90, wherein the hybridizing step comprising hybridizing the target sequence and a second target sequence to the array, and the relative specific binding of the probes from the first group indicates that the target is identical to the first reference sequence, and the relative specific binding of the probes from the second group indicates that the second target sequence is identical to the second reference sequence.

92. The method of claim 90, wherein the first and second target sequences are heterozygous alleles.

REMARKS

The Examiner notes that the previous claims were also pending in commonly owned case 09/164,068. The previous claims have been cancelled and are being pursued in the '068 application. A new set of claims is now provided. Because the present claims are directed to different subject matter than the previous claims, it is recognized that the Examiner will have